



# THE CHANGE IN RUBELLA AND CYTOMEGALOVIRUS SEROPOSITIVITY RATES IN PREGNANT SYRIAN REFUGEES ACCORDING TO YEARS AND COMPARED TO THE LOCAL POPULATION IN KAHRAMANMARAS

Kahramanmaraş'ta Suriyeli mülteci gebelerdeki Rubella ve Sitomegalovirüs seropozitivite oranının yıllara ve yerel halka göre değişiminin araştırılması

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## Abstract

We aimed to evaluate the rates of Rubella and Cytomegalovirus congenital infection agents in pregnant Syrian refugees and to compare these with the local population infection rates over time to determine whether or there was compatibility with the region of settlement. A retrospective examination was made of the Rubella and Cytomegalovirus seroprevalence in all pregnant patients who presented at our hospital for normal prenatal follow-up between January 2012 and July 2021. The pregnant women were grouped as local population and Syrian refugees, and in year groups of 2012-2016, and 2017-2021. The results were compared proportionally according to the time periods. In the 2012-2016 time period, the rubella IgM and IgG seropositivity of the Syrian patients was determined to be statistically significantly higher than that of the local population ( $p=0.013$ ,  $p=0.003$ , respectively). When evaluated in the first and second time periods, there was seen to be a statistically significant proportional decrease in the rubella IgM and IgG seropositivity of the Syrian patients ( $p=0.006$ ,  $p=0.005$ , respectively). When the groups were compared in respect of CMV IgM seropositivity, there was seen to be a significant difference between the groups in the first period ( $p=0.011$ ). The change over time in the Syrian refugees was statistically significant ( $p=0.026$ ). In the second time period, the difference between the Syrian refugees and the local population was not statistically significant ( $p=0.793$ ). In the period of 2012 to 2016, when there was a great increase in the wave of Syrian refugees into Turkey, the seropositivity rates were seen to be significantly high in comparison with the local population. In the second time period examined in this study, there was determined to have been a significant decrease in the rates, most likely in parallel with the access to better living conditions in that time.

**Keywords:** Seroprevalence, Rubella, Cytomegalovirus.

## Özet

Suriyeli mülteci gebelerde konjenital enfeksiyon ajanları olan Rubella ve Sitomegalovirüsün zaman içerisinde yerel popülasyon enfeksiyon oranları ile karşılaştırılarak buldukları bölgeye uyum gösterip göstermediğinin değerlendirilmesi amaçlanmıştır. Ocak 2012-Temmuz 2021 tarihleri arasında normal gebelik takibi amacıyla hastanemize başvuran 16-49 yaş arasındaki tüm gebelerde Rubella, ve Sitomegalovirüs seroprevalansı sonuçları retrospektif olarak araştırıldı. Gebeler yerel halk ve Suriyeli mülteciler olarak gruplandırıldı ve hastalar 2012-2016, 2017-2021 yılları olarak iki periyoda ayrıldı. Sonuçlar zaman periyoduna göre oransal olarak karşılaştırıldı. Çalışmamızda Suriyeli hastalarda 2012-2016 yılları arasında yerel nüfus ile karşılaştırıldığında hem Rubella IgM hem de IgG seropozitifliğinin anlamlı oranda yüksek olduğu görüldü (sırasıyla  $p=0,013$ ,  $p=0,003$ ). Suriyeli mülteci gebeler zamansal olarak ilk ve ikinci periyoda Rubella IgM hem de IgG seropozitifliği açısından değerlendirildiğinde oransal olarak anlamlı azalma olduğu görüldü (sırasıyla  $p=0,006$ ,  $p=0,005$ ). Gruplar CMV IgM seropozitifliği açısından değerlendirildiğinde Suriyeli ve yerel gebe popülasyon arasında ilk periyotta görülen seropozitiflik oranlarının anlamlı farklı olduğu ( $p=0,011$ ) görüldü. Ek olarak Suriyeli mültecilerde zamansal değişimin anlamlı oranda farklı olduğu ( $p=0,026$ ) ancak ikinci periyotta mülteciler ve yerel halk arasındaki farkın anlamsız olduğu görüldü ( $0,793$ ). Suriyeli mültecilerde göç dalgasının ciddi düzeyde olduğu 2012 ve 2016 yılları arasında yerel popülasyonla karşılaştırıldığında anlamlı oranda yüksek olan seropozitiflik oranlarının ikinci dönemde mültecilerin muhtemel daha iyi şartlara erişimine paralel olarak anlamlı oranda düşüş gösterdiği belirlendi.

**Anahtar kelimeler:** Seroprevalans, Rubella, Sitomegalovirüs.

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## Introduction

Rubella and Cytomegalovirus (CMV), which are agents that can cause congenital infections and anomalies, are an important cause of perinatal morbidity and mortality in under-developed and developing countries (1, 2). Although these infection agents, which can be seen in all age groups, generally have an asymptomatic course in the community, they can cause congenital malformations in the fetus if a pregnant woman becomes infected, especially in the first trimester (3).

Rubella infection in the mother and in childhood has a mild clinical course resembling measles, but in a fetus can lead to severe problems, and is a viral infection disease that can be prevented with vaccination (4, 5). CMV is the most common viral agent causing congenital infection, which may cause sequelae such as mental retardation, chorioretinitis, and cerebral calcification in the fetus (6, 7).

Previous studies have shown that one of the factors affecting the spread of these type of infection agents is the level of

development of the country or region (4-7).

The civil war in Syria started on 15 March 2011 and has thus been going on for more than 10 years. As Syria shares a border with Turkey, during that time many refugees have entered and settled in Turkey. Since then, studies conducted especially in our region and city have reported higher rates of these agents, which are in the TORCH group (Toxoplasmosis, Rubella, Cytomegalovirus and Herpes simplex virus) in refugees compared to the local population (8). However, no study could be found in literature which has examined whether or not there has been any positive or negative change in the frequency of these infectious agents in refugees in this extended period.

The aim of this study was to determine any change in the rubella and CMV seropositivity rates in pregnant Syrian refugees who settled in the province of Kahramanmaraş in the early and late waves of migration, and to compare these rates with those of the local population.

## Methods

A retrospective screening was made of patient files in the hospital automated records system for the Rubella and CMV IgG and IgM antibody results in the serum samples taken from patients aged 16-49 years in the first trimester of pregnancy who presented at the Obstetrics and Gynaecology Polyclinic of Kahramanmaraş Necip Fazıl City Hospital between January 2012 and July 2021. The age and serological results were recorded for each patient. Approval for the study was granted by the Clinical Research Ethics Committee of Kahramanmaraş Sutcu Imam University (decision no: 14 session: 29/06/2021). The study was conducted in accordance with the principles of Helsinki Declaration.

Rubella and CMV IgG and IgM antibody tests were performed on the venous blood samples of all the patients using a micro ELISA device. The seropositivity rates

were determined within the two time periods of 2012-2016 and 2017-2021, and these rates were compared between Syrian refugees and the local population and separately within each population group between the two time periods. In the case of any repeated results found by scanning all the blood sample results, only the results from the first presentation were included in the analysis, and the patients were evaluated as a single group.

**Statistical analysis:** Data obtained in the study were analyzed statistically using SPSS v. 17.0 software (IBM Corp., Armonk, NY, USA). The conformity of continuous data to normal distribution was assessed with the Kolmogorov-Smirnov test. Quantitative variables were stated in the tables as mean±standard deviation (SD) and median, range (minimum-maximum) values, and

categorical variables as number (n) and percentage (%). In comparisons of multiple cell tables, the Chi-square test was used. A

value of  $p < 0.05$  was accepted as statistically significant.

## Results

In the 10-year period of the study, rubella was examined in a total of 60,788 serum samples, and CMV in 44,301 samples. In the 2012-2016 time period, the rubella IgM and IgG seropositivity of the Syrian patients was determined to be statistically significantly higher than that of

the local population ( $p=0.013$ ,  $p=0.003$ , respectively). There was seen to be a statistically significant proportional decrease in the rubella IgM and IgG seropositivity of the Syrian patients when evaluated in the first and second time periods, ( $p=0.006$ ,  $p=0.009$ , respectively) (Table 1).

**Table 1:** Periodic comparisons of the Rubella infection agent in the two groups.

	Rubella IgM (+)			Rubella IgG (+)		
	Syrian refugees (n, %)	Turkish Women (n, %)	p	Syrian refugees (n, %)	Turkish Women (n, %)	p
2012-2016 Age (years)	26.00±7.48	26.00±7.48	0.286	25.99±6.15	26.03±6.39	0.792
2017-2021 Age (years)	25.83±6.63	25.83±6.63	0.417	24.78±5.26	25.37±6.48	0.764
p	0.251	0.523		0.361	0.628	
2012-2016 n,%	91 (%3.6)	490 (%2.2)	0.013	519 (%75.4)	6622 (%94.7)	0.003
2017-2021 n,%	53 (%2.3)	448 (%2.1)	0.438	358 (%89.1)	4338 (%93.9)	0.470
p	<b>0.006</b>	0.375		<b>0.009</b>	0.563	

When the groups were compared in respect of CMV IgM seropositivity, there was seen to be a significant difference between the groups in the first period ( $p=0.011$ ). The change over time in the Syrian refugees was

statistically significant ( $p=0.026$ ). In the second time period, the difference between the Syrian refugees and the local population was not statistically significant ( $p=0.793$ ) (Table 2).

**Table 2:** Periodic comparisons of the CMV infection agent between the local population and the Syrian refugees.

	CMV IgM (+)			CMV IgG (+)		
	Syrian refugees (n, %)	Turkish Women (n, %)	p	Syrian refugees (n, %)	Turkish Women (n, %)	p
2012-2016 Age (years)	25.62±6.21	25.21±6.14	0.908	25.32±6.15	26.53±6.29	0.721
2017-2021 Age (years)	25.32±6.66	26.01±6.00	0.581	26.39±6.41	26.08±6.56	0.834
p	0.921	0.671		0.529	0.731	
2012-2016 n,%	40 (%4.7)	382 (%3.2)	<b>0.011</b>	1442 (%99.9)	6582 (%97.5)	0.494
2017-2021 n,%	56 (%3.3)	364 (%3.1)	0.793	1879 (%97.9)	7784 (%97.8)	0.967
p	<b>0.026</b>	0.846		0.587	0.930	

## Discussion

There are few studies in literature which have evaluated the community adaptation of refugees in respect of prenatal and perinatal infection agents. To briefly summarise the study results, Rubella and CMV infections which can lead to severe fetal anomalies, were seen at a significantly higher rate in the pregnant Syrian refugees than in the local pregnant population in the first 5-year period of 2012-2016. However, in the second period of 2017-2021, the difference between the groups was not statistically significant. The reason for this change was thought to be that over the years, the Syrian refugees had achieved better living conditions, moving from tented camps to normal settled accommodation, and having reached a better economic level.

Rubella, which can be seen in any age group, but is most frequent in childhood, can cause severe fetal anomalies in pregnancy. Although congenital rubella syndrome usually causes hearing loss in the fetus, there may also be obstetric problems such as retarded intrauterine development, prematurity, and abortus. Therefore, the desired status for women in the reproductive years is to be seropositive against rubella (9,

10). Rubella seropositivity in reproductive age women has been reported to vary between 70% and 99% (11). It has been recommended that an immunity level of 90% should be achieved in the target mothers to be able to bring congenital rubella syndrome under control. In Turkey, rubella vaccinations have been routinely administered since 2006 (12). Studies conducted in different regions of Turkey have reported Rubella IgM seropositivity as 0%-1.9% and IgG seropositivity as 76.5%-99.5% in women of reproductive age (11-14). However, the most striking point of these studies is that IgG seropositivity was found to be >95% in regions with a high level of development and around 75% in the regions in the east of Turkey which have a low level of development. The results of the current study showed Rubella IgG seropositivity rates of approximately 94% in the local population in both time periods, and the difference from the rates of the refugees was statistically significant in the first 5-year period ( $p=0.003$ ). In the second time period, the results of both groups were similar, with no statistically significant difference determined ( $p=0.470$ ). This was thought to

be the result of the vaccination program applied to the refugees.

The spread of CMV, which can cause retarded growth, microcephaly, chorioretinitis, hepatitis and anemia in the fetus, has been closely associated with the socioeconomic level of the community (15). Although seropositivity rates vary according to global regions, the rate may be as high as 100% in underdeveloped countries and women of low socioeconomic level (16). In studies conducted in various regions of Turkey, CMV IgM seropositivity rates have been reported to vary between 0.4% and 3.2%, and IgG rates between 94.9% and 99.5% (8,12-14, 17). It is noticeable that rates are higher in under-developed regions and border regions with a large refugee population (12, 13). In the first period of the current study, the CVM IgM seropositivity rate of 3.2% in the local population was similar to the findings of a previous study in this city by Bakacak et al (8), and in the same period the rate of the Syrian refugees was determined to be significantly lower ( $p=0.011$ ). However, in the second period, the seropositivity rates of the Syrian refugees fell significantly ( $p=0.026$ ) and were seen to

be similar to those of the local population ( $p=0.793$ ).

The main limitation of this study was the retrospective design. However, as there has been an electronic records system in our hospital for the last ten years, data loss was thought to be minimal and this was not considered to have created a serious problem. A strong aspect of this study was the large number of patients evaluated.

In the period of 2012 to 2016, when there was a great increase in the wave of Syrian refugees in to Turkey, the CMV seropositivity rates were seen to be significantly high in comparison with the local population. In the second time period examined in this study, there was determined to have been a significant decrease in the rates, most likely in parallel with the access to better living conditions in that time. As a result of the positive effect of the vaccination programs applied to refugees, there was determined to be a significant increase in the Rubella IgG seropositivity rates. Therefore, the results of this study clearly showed that better living conditions achieved by refugees can cause a reduction in infectious agents that cause congenital abnormalities.



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